

Y-Z is -CH₂CH₂- or -CONR³-;

A is O or NR¹;

m is 0 or 1;

R¹ is hydrogen or C₁₋₃ alkyl;

each non-aromatic ring carbon atom is unsubstituted or independently substituted with one or two R² substituents and each aromatic ring carbon atom is unsubstituted or independently substituted with one R² substituent selected from the group consisting of

C₁₋₈ alkyl, C₃₋₈ cycloalkyl,
C₃₋₈ cycloheteroalkyl, C₃₋₈ cycloalkyl-C₁₋₆ alkyl,
C₃₋₈ cycloheteroalkyl-C₁₋₆ alkyl, aryl, aryl-C₁₋₆ alkyl, amino,
amino-C₁₋₆ alkyl, C₁₋₃ acylamino, C₁₋₃ acylamino-C₁₋₆ alkyl,
(C₁₋₆ alkyl)₁₋₂ amino, C₃₋₆ cycloalkyl-C₀₋₂ amino,
(C₁₋₆ alkyl)₁₋₂ amino-C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₄ alkoxy-C₁₋₆ alkyl,
hydroxycarbonyl, hydroxycarbonyl-C₁₋₆ alkyl, C₁₋₃ alkoxycarbonyl,
C₁₋₃ alkoxycarbonyl-C₁₋₆ alkyl, hydroxy, hydroxy-C₁₋₆ alkyl,
nitro, cyano, trifluoromethyl, trifluoromethoxy, trifluoroethoxy,
C₁₋₈ alkyl-S(O)₀₋₂, (C₁₋₈ alkyl)₀₋₂ aminocarbonyl,
C₁₋₈ alkyloxycarbonylamino, (C₁₋₈ alkyl)₁₋₂ aminocarbonyloxy,
(aryl C₁₋₃ alkyl)₁₋₂ amino, (aryl)₁₋₂ amino,
aryl-C₁₋₃ alkylsulfonylamino, and C₁₋₈ alkylsulfonylamino;

or two R² substituents, when on the same non-aromatic carbon atom, are taken together with the carbon atom to which they are attached to form a carbonyl group, or two R² substituents, together with the carbon atoms to which they are attached, join to form a 3- to 6-membered saturated spiro-carbocyclic ring;

R³ is hydrogen or C₁₋₄ alkyl;

R⁴ is aryl wherein the aryl group is selected from the group consisting of

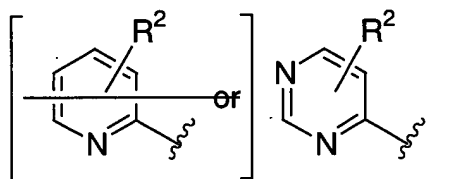
- (1) phenyl,
- (2) naphthyl,
- (3) pyridinyl,
- (4) furyl,

- (5) thienyl,
- (6) pyrrolyl,
- (7) oxazolyl,
- (8) thiazolyl,
- (9) imidazolyl,
- (10) pyrazolyl,
- (11) isoxazolyl,
- (12) isothiazolyl,
- (13) pyrimidinyl,
- (14) pyrazinyl,
- (15) pyridazinyl,
- (16) quinolyl,
- (17) isoquinolyl,
- (18) benzimidazolyl,
- (19) benzofuryl,
- (20) benzothienyl,
- (21) indolyl,
- (22) benzthiazolyl,
- (23) benzoxazolyl,
- (24) dihydrobenzofuryl,
- (25) benzo(1,3)dioxolanyl,
- (26) benzo(1,4)dioxanyl, and
- (27) quinoxaliny;

and mono, di, and tri-substituted aryl wherein the substituents are independently hydrogen, hydroxy, hydroxy-C₁₋₆ alkyl, halogen, C₁₋₈ alkyl, C₃₋₈ cycloalkyl, aryl, aryl C₁₋₃ alkyl, amino, amino C₁₋₆ alkyl, C₁₋₃ acylamino, C₁₋₃ acylamino-C₁₋₆ alkyl, C₁₋₆ alkylamino, di(C₁₋₆)alkylamino, C₁₋₆ alkylamino-C₁₋₆ alkyl, di(C₁₋₆)alkylamino-C₁₋₆ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylthio, C₁₋₄ alkylsulfinyl, C₁₋₄ alkylsulfonyl, C₁₋₄ alkoxy-C₁₋₆ alkyl, hydroxycarbonyl, hydroxycarbonyl-C₁₋₆ alkyl, C₁₋₅ alkoxycarbonyl, C₁₋₃ alkoxycarbonyl-C₁₋₆ alkyl, C₁₋₅ alkylcarbonyloxy, cyano, trifluoromethyl, 1,1,1-trifluoroethyl, trifluoromethoxy, trifluoroethoxy, or nitro; or two adjacent substituents together with the carbon atoms to which they are attached join to form a five- or six-membered saturated or unsaturated ring containing 1 or 2 heteroatoms selected from the group consisting of N, O, and S, whose ring carbon atoms may be substituted with oxo or C₁₋₃ alkyl; and

R^5 is hydrogen or C_{1-3} alkyl.

2. (amended) The A compound of Claim 1 wherein X is ~~selected from the group consisting of~~



Y is $-CH_2CH_2-$; and

R^2 , R^4 , and R^5 are as defined in Claim 1.

3. (amended) The A compound of Claim 2 wherein R^4 is mono- or di-substituted

phenyl,
pyridinyl,
quinolyl,
pyrimidinyl,
pyrazinyl,
quinoxalinyl, or
dihydrobenzofuryl;

wherein the substituents are independently hydrogen, hydroxy, hydroxy- C_{1-6} alkyl, halogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, aryl, aryl C_{1-3} alkyl, amino, amino- C_{1-6} alkyl, C_{1-3} acylamino, C_{1-3} acylamino- C_{1-6} alkyl, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{1-6} alkylamino C_{1-6} alkyl, di(C_{1-6})alkylamino- C_{1-6} alkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-4} alkoxy- C_{1-6} alkyl, hydroxycarbonyl, hydroxycarbonyl- C_{1-6} alkyl, C_{1-5} alkoxycarbonyl, C_{1-3} alkoxycarbonyl C_{1-6} alkyl, C_{1-5} alkylcarbonyloxy, cyano, trifluoromethyl, 1,1,1-trifluoroethyl, trifluoromethoxy, trifluoroethoxy, or nitro; or two adjacent substituents together with the carbon atoms to which they are attached join to form a five- or six-membered

saturated or unsaturated ring containing 1 or 2 heteroatoms selected from the group consisting of N, O, and S, whose ring carbon atoms may be substituted with oxo or C₁₋₃ alkyl.

4. (amended) ~~The~~ A compound of Claim 3 wherein R⁴ is mono- or di-substituted

pyridinyl,
quinolyl,
pyrimidinyl,
pyrazinyl,
quinoxalinyl, or
dihydrobenzofuryl;

wherein the substituents are independently hydrogen, halogen, phenyl, C₁₋₄ alkyl, C₃₋₆ cycloalkyl, C₁₋₃ alkoxy, amino, C₁₋₃ alkylamino, di(C₁₋₃) alkylamino, hydroxy, cyano, trifluoromethyl, 1,1,1-trifluoroethyl, trifluoromethoxy, or trifluoroethoxy.

5. (amended) ~~The~~ A compound of Claim 4 wherein R² is selected from ~~the~~ ~~group consisting of~~

hydrogen,
amino,
C₁₋₄ alkylamino,
C₃₋₆ cycloalkyl-C₀₋₂ alkylamino
cyano,
C₁₋₄ alkyl,
cyclopropyl,
aryl C₁₋₃ alkyl,
C₁₋₄ acylamino,
C₁₋₄ alkoxy,
C₁₋₄ alkylthio,
aminocarbonyl,
(C₁₋₆ alkyl)₁₋₂ aminocarbonyl,
C₁₋₄ alkoxycarbonyl,
trifluoromethyl, and
trifluoromethoxy.

6. (amended) The A compound of Claim 5 wherein R² is selected from the group consisting of

hydrogen,
amino,
C₁₋₃ alkylamino,
C₃₋₆ cycloalkylmethylamino,
C₁₋₄ alkyl,
cyclopropyl,
trifluoromethyl, and
trifluoromethoxy.

7. (amended) The compound of Claim 1 selected from the group consisting of:

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino}-3-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino-3(R)-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(2,4-Diaminopyrimidin-6-yl)pentanoyl]-(N-methyl)amino-3(S)-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3(R)-(6-methoxypyridin-3-yl)-propanoic acid;

{[5-(3-Amino-5,6,7,8-tetrahydroisoquinolin-1-yl)pentanoyl]-(N-methyl)amino}-3(S)-(6-methoxypyridin-3-yl)-propanoic acid;

~~3-(5-(3,4-Dihydro-2H-pyrido[3,2-b][1,4]oxazin-6-yl-pentanoylamino)-3-(quinolin-3-yl)-propionic acid;~~

~~3-(5-3,4-Dihydro-2H-pyrido[3,2-b][1,4]oxazin-6-yl-pentanoylamino)-3(R)-(quinolin-3-yl)-propionic acid;~~

~~3-(5-3,4-Dihydro-2H-pyrido[3,2-b][1,4]oxazin-6-yl-pentanoylamino)-3(S)-(quinolin-3-yl)-propionic acid;~~

~~3-(Quinolin-3-yl)-3-(5-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazin-6-yl-pentanoylamino)-propionic acid;~~

~~3(R)-(Quinolin-3-yl)-3-(5-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazin-6-yl-pentanoylamino)-propionic acid;~~

~~3(S)-(Quinolin-3-yl)-3-(5-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazin-6-yl-pentanoylamino)-propionic acid;~~

~~9-(6-Methylamino-pyridin-2-yl)-3-(pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Methylamino-pyridin-2-yl)-3(R)-(pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Methylamino-pyridin-2-yl)-3(S)-(pyrimidin-5-yl)-nonanoic acid;~~

9-(2,4-Diaminopyrimidin-6-yl)-3-(quinolin-3-yl)-nonanoic acid;

9-(2,4-Diaminopyrimidin-6-yl)-3(R)-(quinolin-3-yl)-nonanoic acid;

9-(2,4-Diaminopyrimidin-6-yl)-3(S)-(quinolin-3-yl)-nonanoic acid;

3-(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

3(R)-(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

3(S)-(2-Methyl-pyrimidin-5-yl)-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

3-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

3(R)-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

3(S)-Pyrimidin-5-yl-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin-2-yl)-nonanoic acid;

(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

3(R)-(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

3(S)-(2-Methyl-pyrimidin-5-yl)-9-(1,4,5,6-tetrahydro-pyrimidin-2-ylcarbamoyl)-nonanoic acid;

~~9-(6-Methylamino-pyridin-2-yl)-3-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Methylamino-pyridin-2-yl)-3(R)-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Methylamino-pyridin-2-yl)-3(S)-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~3-(2-Methoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~3(R)-(2-Methoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~3(S)-(2-Methoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~3-(2-Ethoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~3(R)-(2-Ethoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~3(S)-(2-Ethoxy-pyrimidin-5-yl)-9-(6-methylamino-pyridin-2-yl)-nonanoic acid;~~

~~9-(6-Ethylamino-pyridin-2-yl)-3-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Ethylamino-pyridin-2-yl)-3(R)-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~9-(6-Ethylamino-pyridin-2-yl)-3(S)-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~

~~3-(2-Methoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~
~~3(R)-(2-Methoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~
~~3(S)-(2-Methoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~
~~3-(2-Ethoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~
~~3(R)-(2-Ethoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~
~~3(S)-(2-Ethoxy-pyrimidin-5-yl)-9-(6-ethylamino-pyridin-2-yl)-nonanoic acid;~~

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(dihydrobenzofuran-6-yl)-nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(dihydrobenzofuran-6-yl)-nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(dihydrobenzofuran-6-yl)-nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(6-methoxypyridin-3-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(6-methoxypyridin-3-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(6-methoxypyridin-3-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-methoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-methoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-methoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3-(quinoxalin-2-yl)nonanoic acid;
9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(R)-(quinoxalin-2-yl)nonanoic acid;

9-(4-Amino-2-ethylaminopyrimidin-6-yl)-3(S)-(quinoxalin-2-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Amino-4-ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3(R)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(4-Amino-2-aminopyrimidin-6-yl)-3(S)-(2-methylpyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3(R)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
9-(2-Ethylaminopyrimidin-6-yl)-3(S)-(2-ethoxypyrimidin-5-yl)nonanoic acid;
~~9-(6-Methylamino-pyridin-2-yl)-3-quinoxalin-2-yl-nonanoic acid;~~
~~3(R)-9-(6-Methylamino-pyridin-2-yl)-3-quinoxalin-2-yl-nonanoic acid;~~
~~3(S)-9-(6-Methylamino-pyridin-2-yl)-3-quinoxalin-2-yl-nonanoic acid;~~
~~9-(2,3-Dihydro-1H-pyrrolo[2,3-b]pyridin-6-yl)-3-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~
~~3(R)-9-(2,3-Dihydro-1H-pyrrolo[2,3-b]pyridin-6-yl)-3-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~
~~3(S)-9-(2,3-Dihydro-1H-pyrrolo[2,3-b]pyridin-6-yl)-3-(2-methyl-pyrimidin-5-yl)-nonanoic acid;~~
and
3-(2-Methyl-pyrimidin-5-yl)-10-(1,4,5,6-tetrahydro-pyrimidin-2-ylamino)-decanoic acid;
or a pharmaceutically acceptable salt thereof.

8. (canceled)

9. (original) A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier.

10. (original) The composition of Claim 9 which further comprises an active ingredient selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) an androgen receptor modulator,
- d) a cytotoxic/antiproliferative agent,
- e) a matrix metalloproteinase inhibitor,
- f) an inhibitor of epidermal-derived, fibroblast-derived, or platelet-derived growth factors,
- g) an inhibitor of VEGF,
- h) an antibody to a growth factor or a growth factor receptor,
- i) an inhibitor of Flk-1/KDR, Flt-1, Tck/Tie-2, or Tie-1,
- j) a cathepsin K inhibitor,
- k) a growth hormone secretagogue,
- l) an inhibitor of osteoclast proton ATPase,
- m) an inhibitor of urokinase plasminogen activator (u-PA),
- n) a tumor-specific antibody-interleukin-2 fusion protein,
- o) an inhibitor of HMG-CoA reductase, and
- p) a farnesyl transferase inhibitor or a geranylgeranyl transferase inhibitor or a dual farnesyl/geranylgeranyl transferase inhibitor; and mixtures thereof.

11. (original) The composition of Claim 10 wherein said active ingredient is selected from the group consisting of

- a) an organic bisphosphonate or a pharmaceutically acceptable salt or ester thereof,
- b) an estrogen receptor modulator,
- c) an androgen receptor modulator,
- d) a cathepsin K inhibitor,
- e) an HMG-CoA reductase inhibitor, and
- f) an inhibitor of osteoclast proton ATPase; and mixtures thereof.

12. (original) The composition of Claim 11 wherein said organic bisphosphonate or pharmaceutically acceptable salt or ester thereof is alendronate monosodium trihydrate.

13. (original) A method of eliciting an α_v integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

14. (original) The method of Claim 13 wherein α_v the integrin receptor antagonizing effect is an $\alpha_v\beta_3$ antagonizing effect.

15. (original) The method of Claim 14 wherein the $\alpha_v\beta_3$ antagonizing effect is selected from the group consisting of inhibition of bone resorption, restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

16. (original) The method of Claim 15 wherein the $\alpha_v\beta_3$ antagonizing effect is the inhibition of bone resorption.

17. (original) A method of treating or preventing osteoporosis in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1.

18. (original) The method of Claim 12 wherein the α_v integrin receptor antagonizing effect is an $\alpha_v\beta_5$ antagonizing effect.

19. (original) The method of Claim 18 wherein the $\alpha_v\beta_5$ antagonizing effect is selected from the group consisting of inhibition of restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

20. (original) The method of Claim 13 wherein the α_v integrin receptor antagonizing effect is a dual $\alpha_v\beta_3/\alpha_v\beta_5$ antagonizing effect.

21. (original) The method of Claim 20 wherein the dual $\alpha v\beta 3/\alpha v\beta 5$ antagonizing effect is selected from the group consisting of inhibition of bone resorption, restenosis, angiogenesis, diabetic retinopathy, macular degeneration, inflammatory arthritis, cancer, and metastatic tumor growth.

22. (original) A method of eliciting an αv integrin receptor antagonizing effect in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 9.

23. (original) A method of treating or preventing a condition mediated by antagonism of an αv integrin receptor in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the composition of Claim 9.

24. (original) A method of treating metastatic tumor growth in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of a compound according to Claim 1 in combination with radiation therapy.